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EXAMINER	
PRIEBE, SCOTT DAVID	
ART UNIT	**PAPER NUMBER**
1632	18

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/784,810	GERRITSEN ET AL.	
	Examiner	Art Unit	
	Scott D. Priebe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-53* is/are pending in the application.

4a) Of the above claim(s) *1-4,15-38,40,41 and 43-53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *5-14,39 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 February 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group III, claims 5-14, 39 and 42 in Paper No. 17 filed 7/3/03 is acknowledged. The traversal is on the ground(s) that independence is a two-prong test and the Office has failed to show that the proteins of SEQ ID NO: 2 and 6 have different modes of operation, functions, or effects, and that the Office has not provided a rationale as to how invention III is used in materially different methods. This is not found persuasive because independence does not require a two-prong test, that the specification fails to show the two proteins are capable of use together is in itself evidence of independence. Furthermore, these two proteins are different, presumably each has its own biological function and effect, and mode of operation. The specification provides no evidence that these two proteins have identical modes of operation, functions, and effects. With respect to materially different methods of using invention III, inventions IX, XIII, and XIX are materially different methods as indicated. For example, the method of group IX does not require the nucleic acid to be in a vector or in a cell, as does the methods of groups XIII or XIX. In addition, each of these methods are practiced with different materials apart from the nucleic acid of group III. The arguments concerning restriction between groups I and II and groups VII-X, XIII-XVI, XIX-XXII, and XXV-XXVI, between groups V and VI and inventions XXV and XXVI, and between inventions VII and VIII, IX and X, etc. are moot since Applicant has not elected any of these groups.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-4, 15-38, 40, 41, and 43-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic

or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 17.

Information Disclosure Statement

The information disclosure statement filed 12/1/02 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein as reference C15 has not been considered, since no copy of GenBank Acc. No. AA232646 has been provided.

Drawings

New corrected drawings are required in this application because the shading in Figure 3 obscures the sequences shown (cannot be printed clearly). Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Claim Objections

Claims 5-14, 39, and 42 are objected to because of the following informalities: The claims are directed in part to a non-elected invention, wherein the nucleic acid sequence

corresponds to SEQ ID NO: 5 or the encoded amino acid sequence corresponds to SEQ ID NO: 6. Also, claim 5 recites a Markush group of an "amino acid sequence." However, group members labeled as (e) and (f) are nucleic acids, not amino acid sequences. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-7, 9-14, 39 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 5 is directed to an isolated nucleic acid molecule comprising a nucleic acid sequence encoding a polypeptide which is the mature form of SEQ ID NO: 2 or a variant thereof differing by up to 15% of its amino acids, or which is fragment of the mature form. The nucleic acid molecule may be a "naturally-occurring allelic nucleic acid variant", or may encode a "naturally-occurring polypeptide variant".

With respect to the "mature form," the specification (page 8, line 12 to page 9, line 3) indicates that a mature form is the result of natural processing of the precursor polypeptide, i.e. the initial translation product. The mature form may differ in amino acid sequence from the

precursor (e.g. SEQ ID NO: 2) by no more than removal of the N-terminal Met or it may differ by removal of a signal peptide. However, the specification does not disclose the mature form of SphK polypeptide of SEQ ID NO: 2. It does not disclose whether in fact the N-terminal Met is removed, nor does it disclose whether SEQ ID NO: 2 includes a signal peptide. Page 90 (lines 23-24) of the specification implies that this SphK does not have a signal peptide since it appears to be a cytoplasmic protein. (A nucleic acid encoding SEQ ID NO: 2 presumably would encode the mature form, since if SEQ ID NO: 2 is a precursor, it presumably would be processed to produce the mature form in human cells.) In summary, the specification does not describe the structure of the mature form of the SphK of SEQ ID NO: 2, nor provide any characteristics which would distinguish it from SEQ ID NO: 2 or a fragment of SEQ ID NO: 2 that is not a mature form of the protein. Consequently, the specification provides no evidence that Applicant was in possession of a nucleic acid that encoded a mature form of SEQ ID NO: 2 that does not encode all of SEQ ID NO: 2.

With respect to naturally occurring variants, the specification (page 14, lines 6-18) indicates only that DNA sequence polymorphisms in the SphK coding sequence "may exist" in the human population due to allelic variation, and that such polymorphisms may give also result in sequence variation in the polypeptides. However, the specification does not disclose whether such natural sequence variation actually does exist, either in the nucleic acid or amino acid sequence, much less provide the structures for the naturally-occurring nucleic acid sequences or polypeptides. While one may envision nucleic acid or amino acid sequences that differ from SEQ ID NO: 1 or 2 by one or more residues, it would require isolating and sequencing the corresponding nucleic acids from potentially all humans that exist in order to determine whether

a given sequence polymorphism was naturally-occurring or not. If one were to provide one of skill in the art with a nucleic acid or amino acid sequence that differed from SEQ ID NO: 1 or 2, respectively, at one or more residues, the specification provides no information that would allow one to determine whether the sequence was naturally-occurring, as opposed to a strictly man-made sequence variant. Consequently, the specification provides no evidence that Applicant was in possession of nucleic acid molecules that are naturally-occurring nucleic acid variants or that encoded naturally-occurring polypeptide variants; or even whether such variants even exist.

The court and the Board have repeatedly held (Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.,18 USPQ2d 1016 (CA FC, 1991); Fiers v. Revel, 25 USPQ2d 1601 (CA FC 1993); Fiddes v. Baird, 30 USPQ2d 1481 (BPAI 1993) and Regents of the Univ. Calif. v. Eli Lilly & Co., 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. It is not sufficient to define DNA solely by its principal biological property, because disclosure of no more than that, as in the instant case, is simply a wish to know the identity of any DNA with that biological property. Naming a type of material generically known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. When one is unable to envision the detailed constitution of a complex chemical compound having a particular function, such as a nucleic acid, so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the nucleic acid has been isolated. Thus, claiming all DNA's that achieve a result without defining what means will do so

is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived.

Claims 5-7, 9-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleic acid sequence encoding SEQ ID NO: 2 or a fragment thereof, does not reasonably provide enablement for a nucleic acid sequence encoding a polypeptide variant of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 39 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly directed to an isolated nucleic acid molecule comprising a nucleic acid sequence which encodes a variant of the polypeptide of SEQ ID NO: 2, wherein the variant may differ from SEQ ID NO: 2 in up to 15% of the amino acid residues of SEQ ID NO: 2. The claims also embrace naturally occurring nucleic acid variants (of SEQ ID NO: 1) and nucleic acids encoding naturally occurring polypeptide variants (of SEQ ID NO: 2), where the variants need not be natural to humans, the source of SEQ ID NO: 1 and 2.

The claims also embrace a nucleic acid sequence which encodes any portion of SEQ ID NO: 2 or a variant of SEQ ID NO: 2, e.g. part (e) of claim 5. There is no restriction upon the size of the "portion," therefore the portion may be as little as a single amino acid. There is also no

restriction on the identity of the "portion," therefore it may be chosen from that portion of a variant which differs from SEQ ID NO: 2. Consequently, claim 5 and others broadly include virtually any nucleic acid molecule comprising coding sequence for any polypeptide, regardless of its structural relationship with SEQ ID NO: 2.

The specification discloses two classes of use for the claimed nucleic acid molecules that either require the molecules to encode an active sphingosine kinase (SphK) or that can be used in hybridization to detect SphK-encoding nucleic acids (see page 8, lines 2-11). The specification does not teach how to use nucleic acids that cannot be used for these two purposes. While one of skill in the art would be able to simply make variant nucleic acids commensurate in scope with these claims without undue experimentation, the specification does not enable how to make nucleic acids that can be used for the disclosed purposes commensurate in scope with the claims without undue experimentation.

Any two polynucleotides that encode a given amino acid sequence can be less than 67% identical to each other if all possible wobble bases are different (depending on how many amino acids that have codons with 2 wobble positions are present). This means that these sequences could differ by more than every third nucleotide. Relative to a specific polynucleotide, e.g. SEQ ID NO: 1, the vast majority of polynucleotides that encode the same amino acid sequence would be closer to 65% identical than to 100% identical to the reference polynucleotide; as the sequence identity decreases, the number of different polynucleotides increases geometrically. In addition, up to 15% of the amino acids encoded by the nucleic acid sequence may differ from the corresponding amino acids of SEQ ID NO: 2, with the result that the nucleic acid sequence may approach as low as 50% sequence identity with SEQ ID NO: 1.

The specification does not identify any target polynucleotides for hybridization other than SEQ ID NO: 1. Polynucleotides which differ at every tenth nucleotide (90% identical), let alone at every third, will not form stable heteroduplexes (Kennell, Prog. Nucl. Acid Res. Mol. Biol. 11: 259-301, 1971, see para. bridging pages 260-261), and certainly will not hybridize at the high stringency conditions required to hybridize to naturally-occurring polynucleotides that encode a given protein such as the human SphK orthologous to SEQ ID NO: 2. Clearly, even if the claimed invention were limited to nucleic acid sequences encoding SEQ ID NO: 2, the vast majority could not be used in hybridization against any target disclosed in the specification, i.e., SEQ ID NO: 1. One skilled in the art would clearly be required to engage in undue experimentation to determine target DNAs for which the inoperative embodiments could be used; the inoperative embodiments being those which would not hybridize to SEQ ID NO: 1 under the disclosed conditions.

The specification discloses a putative biological activity for the polypeptide of SEQ ID NO: 2 as a sphingosine kinase protein. However, the specification provides no teachings on what amino acid sequence modifications, e.g. insertions, deletions and substitutions, would be permissible in a SphK polypeptide that would improve or at least would not interfere with the biological activity or structural features necessary for the biological activity and stability of the protein. The specification (page 17, lines 1-14) teaches that conserved amino acids between SEQ ID NOs: 2, 4, 6, 8, 10, and 12-15 should not be changed, but fails to teach which amino acids can be changed. It is known in the art that even conservative amino acid substitutions can adversely affect proper folding and biological activity if amino acids that are critical for such functions are substituted, and the relationship between the sequence of a polypeptide and its tertiary structure

is neither well understood nor predictable (see Ngo, in The Protein Folding Problem and Tertiary Structure Prediction, Merz et al. (eds.), Birkhauser Boston: Boston, MA, pp. 433 and 492-495, 1994). Rudinger (in Peptide Hormones, Parsons (ed.), University Park Press: Baltimore, MD, pp. 1-7, 1976) discloses that even for peptide hormones, which are much smaller than the SphK protein, that one cannot predict *a priori* variant amino acid sequences for a biologically active polypeptide. Rather one must engage in "case to case painstaking experimental study" to determine active variants (see page 7).

As set forth in In re Fisher, 166 USPQ 18 (CCPA 1970), compliance with 35 USC 112, first paragraph requires:

> that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991), the court ruled that a claim to a large genus of possible genetic sequences encoding a protein with a particular function that needs to be determined subsequent to the construction of the genetic sequences may not find sufficient support under 35 USC 112, 1st para., if only a few of the sequences that meet the functional limitations of the claim are disclosed and if undue experimentation would be required of one skilled in the art for determining other genetic sequences embraced by the claim. This is the case here, where specification discloses only one putative functional amino acid sequences, SEQ ID NO: 2, for a polypeptide having the necessary properties for the disclosed uses, and provides little guidance on obtaining polypeptide variants of SEQ ID NO: 2 which would be suitable. Consequently, excessive trial and error

experimentation would have been required to identify the necessary nucleic acid sequence derivatives encoding a biologically active SphK protein with an amino acid sequence differing from SEQ ID NO: 2 since the amino acid sequence of such polypeptides could not be predicted.

Claims 39 and 42 are directed to pharmaceutical compositions comprising the nucleic acid molecule of claim 5, presumably one which encodes an active SphK. Recitation of "pharmaceutical" is construed to mean that the composition has an intended pharmaceutical use, in this case gene therapy. The specification generally teaches that nucleic acids encoding SphK can be used to treat diseases or conditions characterized by decreased expression of SphK, and provides general guidance on identifying diseases or conditions that may involved aberrant expression of SphK. However, the specification provides no evidence identifying any disease involving aberrant expression of SphK.

The specification states that decreased SphK activity "in some cells" may lead to apoptosis, and mentions that ischemia "may" be treated with a therapeutic that increases SphK activity. The specification provides the speculation that increasing SphK activity may promote cell survival or proliferation, and in the case of ischemia, promote angiogenesis. (Page 84, line 26 to page 85, line 11.) However, the specification (page 84, lines 3-13) also teaches that therapeutics which decrease SphK should be used to inhibit angiogenesis. This contradiction as to the effects of SphK levels on angiogenesis is not resolved in the specification. The speculation as to diseases that may be treated appears to be based upon Xia et al. (J. Biol. Chem. 274(48): 34499-34505, 1999). However, Xia et al. discloses that one particular cancer cell line is sensitive to TNF-α-induced apoptosis due to the lack of concomitant induction of SphK expression, while normal endothelial cells are protected from apoptosis by TNF-α-induced expression of SphK. This finding does not show that SphK activity protects against apoptosis in general. More important in the context of the claimed pharmaceutical compositions, the findings of Xia et al. provide no basis for predicting the effect of abnormal over-expression of SphK in normal

endothelial cells, such as would occur if transfected with a gene therapy vector expressing SphK. There is no evidence of record of sphingosine-1-phosphate, the product of SphK activity, being used to treat any disease.

While the specification provides guidance on the formulation of pharmaceutical compositions, it does not teach which composition(s) are to be used for treating any particular disease, nor does it teach how or where the compositions are to be administered for treatment of a particular disease. The specification provides no working examples showing successful use of the claimed compositions in gene therapy.

Orkin et al. reviews the state of the art of gene therapy before the instant invention was made. The overall conclusions were: 1) gene therapy for each disease would present its own scientific and clinical challenges; 2) no successful gene therapy protocol was known; 3) significant problems remained in all aspects of gene therapy, especially with respect to effective expression vectors; 4) the pathophysiology of diseases to be treated were poorly understood; 5) one cannot predictably extrapolate the result of one animal model, such as mouse, to treatment of a disease in a different animal, such as human; 6) assessment of known gene therapy protocols was hindered by poor gene transfer, reliance on qualitative, rather than quantitative assessments of gene transfer, lack of suitable controls and poor definition of biochemical or disease endpoints; and 7) that gene therapy has been oversold, and the impression that gene therapy is successful is mistaken (pages 1-2). The specification does not teach how the problems recognized in the prior art are to be overcome. It does not provide any basis for understanding the role of SphK, if any, in the pathophysiology of any particular disease. Verma et al. (Nature 389: 239-242, 1997) reiterates the finding in Orkin that not a single successful gene therapy protocol has been described in the art and that lack of efficient gene delivery and sustained expression remained the Achilles heel of gene therapy (see page 239). Rosenberg et al. (Science 287 : 1751, 2000) reported that at the time the instant application was filed, there was still no

unequivocal instance of clinical efficacy with gene therapy, and that those in the field were still guilty of overselling gene therapy, despite a decade of failure.

In summary, the instant specification provides no more than a goal - to use a nucleic acid encoding SphK protein to treat disease. It provides no guidance on how to achieve the goal or to overcome the art-recognized problems in gene therapy, and no working examples. The specification leaves it entirely to one skilled in the art to develop a pharmaceutical use for the claimed invention. A patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. Tossing out the germ of an idea does not constitute an enabling disclosure. While every aspect of a generic claim need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the skilled artisan to understand and carry out the invention. It is true that a specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. The rule that a specification need not disclose that which is well known in the art simply means that omission of minor details does not cause a specification to fail the enablement requirement, and is not a substitute for an enabling disclosure. However, if there is no disclosure of starting materials and of conditions under which the process can be carried out, undue experimentation is required. Failure to provide such teachings can not be rectified by asserting that the disclosure of the missing necessary information was well known in the prior art. See *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 101, 1005 (CA FC, 1997). In this case, the prior art is of little or no help at all since those in the art had been unsuccessful in achieving any unequivocal instance of effective treatment with gene therapy.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5-14, 39 and 42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 recites the limitation "said mature form" in line 3 of part (d) and line 5 of part (e). There is insufficient antecedent basis for this limitation in the claim. Parts (a) and (b) of claim 5 refer to different members of the group, and parts (d) and (e) do not refer back to parts (a) and (b), which therefore cannot provide the antecedent basis. It is not clear whether reference to "mature form" in parts (d) and (e) was intentional.

Claim 11 is confusing. Claim 11 must have all the limitations of claim 5 from which it depends. Claim 5 uses the term "nucleic acid sequence" to designate a group of sequences as set forth in parts (a)-(f). Claim 11 then uses the term "nucleotide sequence", and it is unclear if the "nucleotide sequence" is the "nucleic acid sequence" of claim 5, or some additional sequence in the "nucleic acid molecule". Also, part (a) of claim 11 recites "first nucleotide sequence" and claim 11 does not recite a "second nucleotide sequence"; while part (b) recites "second polynucleotide." This shift in terminology is confusing, and its significance unclear. The only "amino acid sequence" disclosed in claim 5 is either SEQ ID NO: 2 (or 6). Possible coding sequences for SEQ ID NO: 2 can already differ from one another by up to about 35% of nucleotides in wobble positions. The nucleic acid molecule of claim 5 may also encode a variant of the amino acid sequence, which differs by no more than 15% from SEQ ID NO: 2 (or 6). Consequently, claim 11 permits the coding sequence for the variants to differ by no more than 20% from any of the possible nucleic acid sequence encoding SEQ ID NO: 2 (or 6). Furthermore, the terms "said coding sequence" in line 5 of part (a) and "the first

polynucleotides" in part (b) lack proper antecedent basis. Part (a) recites two different coding sequences, one is of the first nucleotide sequence and the second is of the coding sequence of the amino acid sequence.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 5-7, 9-14, 39 and 42 are rejected under 35 U.S.C. 102(a) as being anticipated by Young et al., WO 98/54963. (The copy provided to Applicant lacks those parts of the Sequence Listing which do not pertain to the relied upon sequences.)

Young et al. discloses a nucleic acid molecule comprising a nucleic acid sequence (SEQ ID NO: 90, pages 343-344), disclosed as encoding an amino acid sequence (SEQ ID NO: 313, pages 523-524). Nucleotides 1-1498 of SEQ ID NO: 90 of Young is 97.8% identical to nucleotides 102-1600 of instant SEQ ID NO: 1, and 91.2% identical to all SEQ ID NO: 1. SEQ ID NO: 313 of Young is 96.6% identical to amino acids 92-384 of instant SEQ ID NO: 2. Consequently, SEQ ID NO: 90 of Young comprises an allelic nucleic acid fragment of instant SEQ ID NO: 1 encoding at least a portion of a naturally-occurring variant of SEQ ID NO: 2, which differs in less than 15% of amino acids, and the coding sequence for SEQ ID NO: 313 differs in less than 20% of nucleotides from the corresponding region of SEQ ID NO: 1. Young

discloses vectors comprising the nucleic acid sequence under control of a promoter, cells containing vector, and use of the nucleic acid in gene therapy (thus implying a pharmaceutical composition) (pages 171, 202-203, 206, 233-235, 262-264; pages 765-766, claims 1, 3, 4, 7-10). Also, claims 39 and 42 directed to "pharmaceutical" compositions do not distinguish from the prior art nucleic acid compositions used for other purposes, such as for use of the nucleic acid molecule for transfection of cultured mammalian cells (page 233-235).

Claims 5-7, 9, 11-14, 39 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated by Kohama et al. (J. Biol. Chem. 273 (37): 23722-23728, 1998), including GenBank Acc. No. AF068748 (1998) cited therein (page 23722, col. 1).

Kohama et al. discloses a nucleic acid sequence (GenBank Acc. No. AF068748) encoding the murine SphK1a protein (Fig. 1, page 23724). The murine SphK1a nucleic acid sequence comprises a fragment encoding "at least a portion" of the amino acid sequence set forth as SEQ ID NO: 2. For example, amino acid 1 and amino acids 76-108 are identical to amino acid 1 and amino acids 77-109 of SEQ ID NO: 2. Since the nucleic acid sequence is naturally occurring it is also an allelic variant of other murine SphK1a sequences, and encodes a natural polypeptide. With respect to claim 9 or 11, the N-terminal methionine codon meets the fragment option. Kohama discloses vectors comprising the nucleic acid sequence operably linked to a promoter and cells comprising the vector (page 23723, col. 1) for transfection of cultured mammalian cells, and lipofectAMINE compositions which would meet the material limitations of pharmaceutical compositions.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on M-F, 8:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached on 703 305-4051. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Scott D. Priebe
Primary Examiner
Art Unit 1632